IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Bruce A. Yankner and Philip Nadeau

Serial No.: Divisional of 09/239,387

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For: METHODS FOR DECREASING BETA AMYLOID PROTEIN

Box Patent Application
Commissioner of Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Prior to examination, please amend the application as follows.

In the Specification

On page 1, after the title and before the heading "Background of the Invention", please insert the following heading and paragraph.

--Cross-Reference to Related Applications

This application is a divisional of pending prior application U.S. Serial No. 09/239,387 filed January 28, 1999, which is a divisional of U.S. Serial No. 09/046,235 filed March 23, 1998, now U.S. Patent No. 6,080,778. The United States government has certain rights in this invention by virtue of National Institutes of Health grant number RO1NS33325 to Bruce A. Yankner.--

On page 1, lines 3-5, please delete the sentence beginning with "The United States government", and ending with "Bruce A. Yankner."

In the Claims

Please delete claims 1-22.

Remarks

Applicants have enclosed a copy of the claims as pending upon entry of the Preliminary Amendment. Applicants have also enclosed a marked-up version of amended specification page 1 pursuant to 37 C.F.R. § 1.121(b)(1)(iii), and a clean copy of amended specification page 1 pursuant to 37 C.F.R. § 1.121(b)(1)(ii).

Respectfully submitted,

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Claims As Pending Upon Entry of Preliminary Amendment

23. A composition for decreasing the production of Aβ comprising an effective amount of a compound to decrease blood cholesterol levels.

24. The composition of claim 23 comprising an HMG CoA reductase inhibitor.

25. The composition of claim 24 wherein the inhibitor is selected from the group consisting of lovastatin, simvastatin, fluvastatin, pravastatin, atorvastatin, cerivastatin, and compactin.

26. The composition of claim 23 comprising a compound which inhibits uptake of dietary cholesterol.

27. The composition of claim 23 wherein the composition blocks or decreases endogenous cholesterol production.

28. The composition of claim 27 wherein the composition comprises an inhibitor of the cholesterol biosynthetic enzymes selected from the group consisting of 2,3-oxidosqualene cyclase, squalene synthase, and 7-dehydrocholesterol reductase.

29. The composition of claim 23 wherein the composition is selected from the group consisting of a fibrate, a bile acid binding resin, probucol, nicotinic acid, garlic or garlic derivative, and psyllium.

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this paper and any documents referred to as attached or enclosed are being deposited with the United States Postal Service on this date, February 28, 2002, in an envelope as "Express Mail Post Office to Addressee" service under 37 C.F.R. § 1.10, Express Mail Label No. EL 778 571 835 US, addressed to Box Patent Application, Commissioner of Patents and Trademarks, Washington, D.C. 20231.

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Date: February 28, 2002

ATL1 #504917 v1

Marked-up Copy of Amended Specification Page 1
Pursuant to 37 C.F.R. § 1.121(b)(1)(iii)

METHODS FOR DECREASING BETA AMYLOID PROTEIN

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Background of the Invention

[The United States government has certain rights in this invention by virtue of National Institutes of Health grant number RO1NS33325 to Bruce A. Yankner.]

Alzheimer's disease (AD) is the most common cause of dementia in the aged population. The accumulation of large numbers of senile plaques containing the 40-42 amino acid amyloid β protein (Aβ) is a classic pathological feature of AD. Both genetic and cell biological findings suggest that the accumulation of Aβ in the brain is the likely cause of AD (Yankner, B.A. (1996) Neuron 16, 921-932.; Selkoe, D.J. Science 275, 630-631 (1997)). Strong genetic evidence in support of the pathogenic role of Aβ came from the observation that individuals who inherit mutations in the amyloid precursor protein almost invariably develop AD at an early age. These mutations increase the production of a long variant of the Aβ peptide that forms senile plaques in the brain (Goate et al., (1991) Nature 349, 704-706). Mutations and allelic variations in other genes that cause AD, including the presenilins and apolipoprotein E, also result in increased production or deposition of the Aβ peptide. Reiman, et al. (1996) N.E.J.Med. 334, 752-758, reported that in middle age, early to mid 50's, individuals who are homozygous for the Apo E4 gene have reduced glucose metabolism in the same regions of the brain as in patients with Alzheimer's disease. These findings suggest that the pathological changes

Clean Copy of Amended Specification Page 1
Pursuant to 37 C.F.R. § 1.121(b)(1)(ii)

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